

WEST Search History

DATE: Friday, October 01, 2004

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DB=PGPB,USPT; PLUR=YES; OP=OR

<input type="checkbox"/>	L9	L8 and complement?	12
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<input type="checkbox"/>	L4	L3 and gene	74
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<input type="checkbox"/>	L2	L1 and roy	111
<input type="checkbox"/>	L1	curtiss	2793

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Search Results - Record(s) 1 through 10 of 12 returned.

1. Document ID: US 20040101531 A1

Using default format because multiple data bases are involved.

L9: Entry 1 of 12

File: PGPB

May 27, 2004

PGPUB-DOCUMENT-NUMBER: 20040101531

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040101531 A1

TITLE: Immunogenic compositions and vaccines comprising carrier bacteria that secrete antigens

PUBLICATION-DATE: May 27, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
<u>Curtiss, Roy III</u>	St. Louis	MO	US	
Kang, Ho Young	Pusan		KR	

US-CL-CURRENT: 424/184.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KVNC	Drawn Ds
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2. Document ID: US 20030031683 A1

L9: Entry 2 of 12

File: PGPB

Feb 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030031683

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030031683 A1

TITLE: Recombinant vaccines comprising immunogenic attenuated bacteria having Rpos positive phenotype

PUBLICATION-DATE: February 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
<u>Curtiss, Roy III</u>	St. Louis	MO	US	
Nickerson, Cheryl A.	River Ridge	LA	US	

US-CL-CURRENT: 424/200.1; 424/258.1, 424/93.2, 435/252.3, 435/252.8, 435/471, 435/897

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KOMC](#) | [Drawn De](#)

3. Document ID: US 6383496 B1

L9: Entry 3 of 12

File: USPT

May 7, 2002

US-PAT-NO: 6383496

DOCUMENT-IDENTIFIER: US 6383496 B1

TITLE: Recombinant vaccines comprising immunogenic attenuated bacteria having RPOS positive phenotype

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Nickerson; Cheryl A.	River Ridge	LA		

US-CL-CURRENT: 424/200.1; 424/258.1, 424/93.2, 435/252.3, 435/252.8, 435/471,
435/897

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KOMC](#) | [Drawn De](#)

4. Document ID: US 6024961 A

L9: Entry 4 of 12

File: USPT

Feb 15, 2000

US-PAT-NO: 6024961

DOCUMENT-IDENTIFIER: US 6024961 A

TITLE: Recombinant avirulent immunogenic S typhi having rpos positive phenotype

DATE-ISSUED: February 15, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Nickerson; Cheryl A.	Chesterfield	MO		

US-CL-CURRENT: 424/200.1; 424/93.2, 435/252.3, 435/252.8, 435/27, 435/29, 435/4,
435/471

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [Claims](#) | [KOMC](#) | [Drawn De](#)

5. Document ID: US 5855880 A

L9: Entry 5 of 12

File: USPT

Jan 5, 1999

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US-PAT-NO: 5855880

DOCUMENT-IDENTIFIER: US 5855880 A

** See image for Certificate of Correction **

TITLE: Avirulent microbes and uses therefor

DATE-ISSUED: January 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Kelly; Sandra M.	St. Louis	MO		

US-CL-CURRENT: 424/93.2, 424/184.1, 424/200.1, 424/235.1, 424/257.1, 424/258.1,
424/93.48, 435/252.3, 435/252.33, 435/320.1, 435/879

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Search](#) | [Edit](#) | [Claims](#) | [KUMC](#) | [Draw](#) | [De](#)

6. Document ID: US 5855879 A

L9: Entry 6 of 12

File: USPT

Jan 5, 1999

US-PAT-NO: 5855879

DOCUMENT-IDENTIFIER: US 5855879 A

TITLE: Avirulent microbes and uses therefor

DATE-ISSUED: January 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss III; Roy</u>	St. Louis	MO		

US-CL-CURRENT: 424/93.2, 424/184.1, 424/200.1, 424/235.1, 424/257.1, 424/258.1,
424/93.48, 435/252.3, 435/252.33, 435/320.1, 435/879

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Search](#) | [Edit](#) | [Claims](#) | [KUMC](#) | [Draw](#) | [De](#)

7. Document ID: US 5840483 A

L9: Entry 7 of 12

File: USPT

Nov 24, 1998

US-PAT-NO: 5840483

DOCUMENT-IDENTIFIER: US 5840483 A

TITLE: Method of maintaining a desired recombinant gene in a genetic population of cells

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

h e b b g e e e f e ef b e

NAME <u>Curtiss, III; Roy</u>	CITY St. Louis	STATE MO	ZIP CODE	COUNTRY
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US-CL-CURRENT: 435/6; 435/252.3, 435/252.33, 435/320.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Detailed Abstract	Claims	KOMC	Draw. De
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8. Document ID: US 5672345 A

L9: Entry 8 of 12

File: USPT

Sep 30, 1997

US-PAT-NO: 5672345

DOCUMENT-IDENTIFIER: US 5672345 A

TITLE: Selective maintenance of a recombinant gene in a population of vaccine cells

DATE-ISSUED: September 30, 1997

INVENTOR-INFORMATION:

NAME <u>Curtiss, III; Roy</u>	CITY St. Louis	STATE MO	ZIP CODE	COUNTRY
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US-CL-CURRENT: 424/93.2; 435/252.3, 435/69.1, 435/71.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Detailed Abstract	Claims	KOMC	Draw. De
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9. Document ID: US 5656488 A

L9: Entry 9 of 12

File: USPT

Aug 12, 1997

US-PAT-NO: 5656488

DOCUMENT-IDENTIFIER: US 5656488 A

TITLE: Recombinant avirulent salmonella antifertility vaccines

DATE-ISSUED: August 12, 1997

INVENTOR-INFORMATION:

NAME <u>Curtiss, III; Roy</u> Tung; Kenneth S. K.	CITY St. Louis Charlottesville	STATE MO VA	ZIP CODE	COUNTRY
---------------------------------------------------------	--------------------------------------	-------------------	----------	---------

US-CL-CURRENT: 435/252.33; 424/184.1, 424/200.1, 435/252.3, 435/252.8, 435/69.3,
530/395

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Detailed Abstract	Claims	KOMC	Draw. De
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10. Document ID: US 5424065 A

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e ef b e

L9: Entry 10 of 12

File: USPT

Jun 13, 1995

US-PAT-NO: 5424065

DOCUMENT-IDENTIFIER: US 5424065 A

TITLE: Vaccines containing avirulent phop-type microorganisms

DATE-ISSUED: June 13, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Galan; Jorge	St. Louis	MO		

US-CL-CURRENT: 424/93.2; 424/184.1, 424/93.48, 435/252.3, 435/252.8, 435/69.1,
435/71.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Drawn D
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L9: Entry 2 of 12

File: PGPB

Feb 13, 2003

PGPUB-DOCUMENT-NUMBER: 20030031683

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030031683 A1

TITLE: Recombinant vaccines comprising immunogenic attenuated bacteria having RpoS positive phenotype

PUBLICATION-DATE: February 13, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
<u>Curtiss, Roy III</u>	St. Louis	MO	US	
Nickerson, Cheryl A.	River Ridge	LA	US	

US-CL-CURRENT: 424/200.1; 424/258.1, 424/93.2, 435/252.3, 435/252.8, 435/471,
435/897

CLAIMS:

What is claimed is:

1. A method for delivery of a desired gene product to a human comprising: (a) selecting for a strain of bacteria having (i) an RpoS.sup.+ phenotype, (ii) one or more inactivating mutations which render the strain attenuated, and (iii) a recombinant gene encoding the desired gene product; and (b) administering the strain to the human.
2. The method according to claim 1 wherein selecting a strain of bacteria comprises selecting a strain of Salmonella.
3. The method according to claim 2 wherein the strain of Salmonella comprises an inactivating mutation in a mutation in a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, gale, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, slyA, and combinations thereof.
4. The method according to claim 3 wherein the recombinant gene encodes a product from a pathogen to said human.
5. The method according to claim 4 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.
6. The method according to claim 3 wherein the a recombinant gene that encodes a product capable of suppressing, modulating, or augmenting an immune response in said human.
7. The method according to claim 3 wherein the recombinant gene encodes an auto-

antigen.

8. The method according to claim 7 wherein the auto-antigen is a gamete-specific antigen.

9. The method according to claim 3 wherein the recombinant gene encodes an allergen to said human.

10. The method according to claim 3 wherein the recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor-specific antigen.

11. A method for delivery of a desired gene product to a human comprising administering to the human a live attenuated strain of bacteria having (a) a recombinant rpoS.sup.+ gene, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired gene product.

12. The method according to claim 11 wherein administering a strain of bacteria comprises administering a strain of Salmonella.

13. The method according to claim 12 wherein administering a strain of Salmonella comprises administering a strain of S. typhi.

14. The method according to claim 13 wherein the strain of S. typhi comprises an inactivating mutation in a mutation in a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, slyA, and combinations thereof.

15. The method according to claim 14 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

16. The method according to claim 15 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

17. The method according to claim 14 wherein the second recombinant gene encodes a product capable of suppressing, modulating, or augmenting an immune response in said human.

18. The method according to claim 14 wherein the second recombinant gene encodes an auto-antigen.

19. The method according to claim 18 wherein the auto-antigen is a gamete-specific antigen.

20. The method according to claim 14 wherein the second recombinant gene encodes an allergen to said human.

21. The method according to claim 14 wherein the second recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor-specific antigen.

22. A method for producing a strain of carrier microbes for delivery of a desired gene product to a human comprising in any order the steps of: (a) selecting for a strain of bacteria having an RpoS.sup.+ phenotype by performing a test to determine

the RpoS phenotype of the strain; (b) producing one or more inactivating mutations which render the strain attenuated; and (c) introducing into the strain a recombinant gene encoding a desired gene product.

23. The method according to claim 22 wherein selecting for a strain of bacteria comprises selecting for a strain of *Salmonella*.

24. The method according to claim 23 wherein the strain of *Salmonella* comprises an inactivating mutation in a mutation in a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, gale, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, methH, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirc, inv, hilA, hilC, hilD, rpoE, flgM, tonB, slyA, and combinations thereof.

25. The method according to claim 24 wherein the recombinant gene encodes a gene product from a pathogen to said human.

26. The method according to claim 25 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

27. The method according to claim 24 wherein the recombinant gene encodes a product capable of suppressing, modulating, or augmenting an immune response in said human.

28. The method according to claim 24 wherein the recombinant gene encodes an auto-antigen.

29. The method according to claim 28 wherein the auto-antigen is a gamete-specific antigen.

30. The method according to claim 24 wherein the recombinant gene encodes an allergen to said human.

31. The method according to claim 24 wherein the recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor-specific antigen.

32. A method for producing carrier microbes for delivery of a desired gene product to a human comprising generating a strain of bacteria having (a) a recombinant rpoS.sup.+ gene, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired gene product.

33. The method according to claim 32 wherein generating a strain of bacteria comprises generating a strain of *Salmonella*.

34. The method according to claim 33 wherein generating a strain of *Salmonella* comprises generating a strain of *S. typhi*.

35. The method according to claim 34 wherein the strain of *S. typhi* comprises an inactivating mutation in a mutation in a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, gale, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, methH, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirc, inv, hilA, hilC, hilD, rpoE, flgM, tonB, slyA, and combinations thereof.

36. The method according to claim 35 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

37. The method according to claim 36 wherein the pathogen is a virus, bacterium,

protozoan, parasite or fungus.

38. The method according to claim 35 wherein the second recombinant gene encodes a product capable of suppressing, modulating, or augmenting an immune response in said human.

39. The method according to claim 35 wherein the second recombinant gene encodes an auto-antigen.

40. The method according to claim 39 wherein the auto-antigen is a gamete-specific antigen.

41. The method according to claim 35 wherein the recombinant gene encodes an allergen to said human.

42. The method according to claim 35 wherein the second recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor-specific antigen.

43. A carrier microbe for the delivery of a desired gene product to a human comprising a live attenuated bacteria having (a) a recombinant rpoS.sup.+ gene, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired gene product.

44. A carrier microbe according to claim 43 wherein the bacteria comprises a *Salmonella*.

45. A carrier microbe according to claim 44 wherein the *Salmonella* comprises an *S. typhi*.

46. The carrier microbe according to claim 45 wherein the attenuated *S. typhi* comprises an inactivating mutation in a mutation in a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, slyA, and combinations thereof. thereof.

47. The carrier microbe according to claim 46 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

48. The carrier microbe according to claim 47 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

49. The carrier microbe according to claim 46 wherein the second recombinant gene encodes a product capable of suppressing, modulating, or augmenting an immune response in said human.

50. The carrier microbe according to claim 46 wherein the second recombinant gene encodes an auto-antigen.

51. The carrier microbe according to claim 50 wherein the auto-antigen is a gamete-specific antigen.

52. The carrier microbe according to claim 46 wherein the recombinant gene encodes an allergen to said human.

53. The method according to claim 46 wherein the recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor-specific antigen.

54. A composition for immunization of a human comprising a live attenuated strain of bacteria having (a) a recombinant rpoS.sup.+ gene, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired gene product.

55. The composition according to claim 54 wherein the bacteria comprises a Salmonella.

56. The composition according to claim 55 wherein the Salmonella comprises an S. typhi.

57. The composition according to claim 56 wherein the strain of S. typhi comprises an inactivating mutation in a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hild, rpoE, flgM, tonB, slyA, and combinations thereof.

58. The composition according to claim 57 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

59. The composition according to claim 58 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

60. The composition according to claim 57 wherein the second recombinant gene encodes an auto-antigen.

61. The composition according to claim 60 wherein the auto-antigen is a gamete-specific antigen.

62. The composition according to claim 57 wherein the second recombinant gene encodes an allergen to said human.

63. The composition according to claim 57 wherein the recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor-specific antigen.

64. The composition according to claim 54 wherein said attenuated strain of S. typhi is in a pharmaceutically acceptable carrier.

65. A genetically engineered cell comprising a live attenuated strain of bacteria having (a) a recombinant rpoS.sup.+ gene, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired gene product.

66. The genetically engineered cell according to claim 65 wherein the strain of bacteria comprises a strain of Salmonella.

67. The genetically engineered cell according to claim 66 wherein the strain of Salmonella comprises a strain of S. typhi.

68. The genetically engineered cell according to claim 67 wherein the attenuated strain of S. typhi comprises an inactivating mutation in a pab gene,

a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, slyA, and combinations thereof.

69. The genetically engineered cell according to claim 68 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

70. The genetically engineered cell according to claim 69 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

71. The genetically engineered cell according to claim 68 wherein the second recombinant gene encodes a product capable of suppressing, modulating, or augmenting an immune response in said human.

72. The genetically engineered cell according to claim 68 wherein the second recombinant gene encodes an auto-antigen.

73. The genetically engineered cell according to claim 72 wherein the auto-antigen is a gamete-specific antigen.

74. The genetically engineered cell according to claim 68 wherein the recombinant gene encodes an allergen to said human.

75. The method according to claim 68 wherein the recombinant gene encodes a cytokine that suppresses tumor growth and spread, an enzyme that converts a non-toxic prodrug into an anti-tumor drug, or a tumor specific antigen.

76. A method for preparing a vaccine comprising mixing genetically engineered cells according to claim 65 with a pharmaceutically acceptable carrier.

77. A method for delivery of a desired gene product to a human comprising administering to the human a live attenuated strain of bacteria having (a) a recombinant virulence gene which is capable of expressing a gene product that facilitates invasion and colonization of the gut associated lymphoid tissues, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired product.

78. The method according to claim 77 wherein the strain of bacteria is a strain of Salmonella.

79. The method according to claim 78 wherein the strain of Salmonella is a strain of S. typhi.

80. A genetically engineered cell comprising a strain of live attenuated bacteria having (a) a recombinant virulence gene which is capable of expressing a gene product that facilitates invasion and colonization of the gut associated lymphoid tissues, (b) one or more inactivating mutations which render said microbe attenuated and (c) a second recombinant gene encoding the desired product.

81. The genetically engineered cell according to claim 80 wherein the bacteria comprise Salmonella.

82. The genetically engineered cell according to claim 81 wherein the Salmonella comprise S. typhi.

83. A method for assessing the immunogenicity of a bacteria comprising determining the RpoS phenotype of said bacteria wherein the presence of an RpoS.sup.+ phenotype indicates increased immunogenicity compared to an isogenic bacteria having an RpoS.sup.- phenotype.

84. The method of claim 83 wherein the bacteria comprise Salmonella.

85. The method of claim 84 wherein the Salmonella comprise S. typhi.

86. The method of claim 85 wherein the RpoS phenotype is determined by assessing one or both of catalase activity and glycogen biosynthesis activity of the S. typhi.

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L9: Entry 3 of 12

File: USPT

May 7, 2002

US-PAT-NO: 6383496

DOCUMENT-IDENTIFIER: US 6383496 B1

TITLE: Recombinant vaccines comprising immunogenic attenuated bacteria having RPOS positive phenotype

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Nickerson; Cheryl A.	River Ridge	LA		

US-CL-CURRENT: 424/200.1; 424/258.1, 424/93.2, 435/252.3, 435/252.8, 435/471,
435/897

CLAIMS:

What is claimed is:

1. A method for producing, from a parent bacteria strain, a carrier bacteria for the delivery of a desired gene product to a human comprising generating a strain of bacteria comprising (a) a recombinant rpoS.sup.+ gene; (b) one or more inactivating mutations which render said bacteria attenuated; and (c) a second recombinant gene encoding the desired gene product, wherein said carrier bacteria expresses a higher level of RpoS gene product than said parent bacteria strain and wherein said higher level of RpoS gene product confers upon the carrier bacteria high immunogenicity relative to said parent bacteria strain.

2. The method of claim 1, said bacteria lacks a functional chromosomal rpoS.sup.+ gene.

3. The method according to claim 1 wherein the bacteria is a strain of Salmonella.

4. The method according to claim 3 wherein the Salmonella is a strain of S. typhi.

5. The method according to claim 4 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, gale, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

6. The method according to claim 5 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

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7. The method according to claim 6 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

8. A carrier bacteria for the delivery of a desired gene product to a human produced according to the method of claim 1.

9. The carrier bacteria of claim 8, wherein said bacteria lacks a functional chromosomal rpoS+ gene.

10. A carrier bacteria according to claim 8 wherein the bacteria is a Salmonella.

11. A carrier bacteria according to claim 10 wherein the Salmonella is an S. typhi.

12. The carrier bacteria according to claim 11 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, methH, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

13. The carrier bacteria according to claim 12 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

14. The carrier microbe according to claim 13 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

15. A composition for immunization of a human comprising a carrier bacteria according to claim 3.

16. The composition of claim 15, wherein said bacteria lacks a functional chromosomal rpoS+ gene.

17. The composition according to claim 15 wherein the bacteria is a Salmonella.

18. The composition according to claim 17 wherein the Salmonella is an S. typhi.

19. The composition according to claim 18 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, methH, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

20. The composition according to claim 19 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

21. The composition according to claim 20 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

22. The composition according to claim 18 wherein said attenuated strain of S. typhi is in a pharmaceutically acceptable carrier.

23. A genetically engineered bacterial cell, wherein said genetically engineered bacterial cell (a) is produced from a parent bacterial cell, (b) is a live attenuated strain of bacteria, (c) has a recombinant rpoS.sup.+ gene, (d) has one or more inactivating mutations which render said bacteria attenuated and (e) has a second recombinant gene encoding a desired gene product, and wherein the genetically engineered bacterial cell expresses a higher level of RpoS gene product than said parent bacteria cell and wherein said higher level of RpoS gene product confers upon the genetically engineered bacterial cell high immunogenicity relative to said parent bacteria strain.

24. The genetically engineered bacterial cell of claim 23, wherein said bacterial cell lacks a functional chromosomal rpoS+ gene.

25. The genetically engineered bacterial cell according to claim 23 wherein the strain of bacteria is a strain of Salmonella.

26. The genetically engineered bacterial cell according to claim 25 wherein the strain of Salmonella is a strain of S. typhi.

27. The genetically engineered bacterial cell according to claim 26 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, meth, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

28. The genetically engineered bacterial cell according to claim 27 wherein the second recombinant gene encodes a gene product from a pathogen to said human.

29. The genetically engineered bacterial cell according to claim 28 wherein the pathogen is a virus, bacterium, protozoan, parasite or fungus.

30. A method for preparing an immunogenic composition, the method comprising mixing the genetically engineered bacterial cell according to claim 23 with a pharmaceutically acceptable carrier.

31. The method of claim 30, wherein said bacterial cell lacks a functional chromosomal rpoS+ gene.

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L9: Entry 5 of 12

File: USPT

Jan 5, 1999

US-PAT-NO: 5855880

DOCUMENT-IDENTIFIER: US 5855880 A

**** See image for Certificate of Correction ****

TITLE: Avirulent microbes and uses therefor

DATE-ISSUED: January 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Kelly; Sandra M.	St. Louis	MO		

US-CL-CURRENT: 424/93.2, 424/184.1, 424/200.1, 424/235.1, 424/257.1, 424/258.1,
424/93.48, 435/252.3, 435/252.33, 435/320.1, 435/879

CLAIMS:

We claim:

1. An immunogenic composition for the immunization of an individual comprising a derivative of a pathogenic gram negative bacteria made avirulent by an inactivating mutation in a cya gene, in a pharmaceutically acceptable carrier.

2. An immunogenic composition for the immunization of an individual according to claim 1, wherein the avirulent derivative of a pathogenic gram negative bacteria is capable of expressing a recombinant gene derived from an agent which is pathogenic to said individual, to produce an antigen capable of inducing an immune response in said vertebrate against said pathogenic agent.

3. A method for stimulating the immune system to respond to an immunogenic antigen of a pathogenic gram negative bacteria comprising administering to said individual the immunogenic composition of claim 1.

4. A method for stimulating the immune system to respond to an immunogenic antigen of a pathogen comprising administering to said individual the immunoigenic composition of claim 2.

5. An isolated gram negative bacterial strain comprising a derivative of a pathogenic gram negative bacteria made avirulent by an inactivating mutation in a cya gene wherein said derivative is capable of invading and persisting in the gut-associated lymphoid tissue or bronchus-associated lymphoid tissue.

6. The isolated bacterial strain of claim 5 which is capable of expressing a recombinant gene derived from an agent which is pathogenic to an individual, to produce an antigen capable of inducing an immune response in said individual against said pathogenic agent.

7. A strain according to claim 6, wherein the avirulent strain of the pathogenic microbe contains a chromosomal mutation which is lethal, balanced by a vector which complements the lethal mutation to constitute a balanced lethal host-vector system.

8. A strain according to claim 7, wherein cells of the strain:

- a) lack a functioning native chromosomal gene encoding beta-aspartate semialdehyde dehydrogenase (Asd);
- b) have present a recombinant gene encoding a functional Asd polypeptide which complements the chromosomal asd mutation, but which cannot replace the defective chromosomal gene by recombination;
- c) have a physical linkage between the recombinant genes encoding the functional Asd polypeptide and the immunogenic antigen, wherein the loss of the recombinant gene encoding the functional Asd polypeptide causes the cells to lyse when the cells are in an environment in which the lack of functional Asd causes the cells to lyse.

9. A method of utilizing a strain of a pathogenic gram negative bacteria made avirulent by a mutation in a cya gene, the method comprising preparing an immunogenic composition by combining the strain with a pharmaceutically acceptable carrier.

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11. Document ID: US 5387744 A

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L9: Entry 11 of 12

File: USPT

Feb 7, 1995

US-PAT-NO: 5387744

DOCUMENT-IDENTIFIER: US 5387744 A

TITLE: Avirulent microbes and uses therefor: Salmonella typhi

DATE-ISSUED: February 7, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		
Kelly; Sandra M.	St. Louis	MO		

US-CL-CURRENT: 424/258.1; 435/252.3, 435/252.33, 435/320.1, 435/879

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Attachment	Claims	KMNC	Drawn De
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12. Document ID: US 5294441 A

L9: Entry 12 of 12

File: USPT

Mar 15, 1994

US-PAT-NO: 5294441

DOCUMENT-IDENTIFIER: US 5294441 A

**** See image for Certificate of Correction ****

TITLE: Avirulent microbes and uses therefor: salmonella typhi

DATE-ISSUED: March 15, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Curtiss, III; Roy</u>	St. Louis	MO		

US-CL-CURRENT: 424/200.1; 424/235.1, 424/258.1, 435/252.3, 435/252.33, 435/320.1, 435/879

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Attachment	Claims	KMNC	Drawn De
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